REMARKS

I. Status of the Claims

Claims 1, 2, 4-12, 16-21, 23-38, 40-63, 65-67 and 77-91 are pending and under consideration, claims 3, 13-15, 22, 39, 64 and 68-76 having been previously canceled, without prejudice against their reintroduction into this or one or more timely filed continuation, divisional or continuation-in-part applications. Claims 1, 2, 5, 6, 8 and 9 are currently under examination, claims 4, 7, 10-12, 16-21, 23-38, 40-63, 65-67 and 77-91 having been withdrawn as drawn to non-elected subject matter. Claims 1, 8-10, 23, 28, 37 and 89 are amended herewith. Thus, after entry of this Amendment, claims 1, 2, 4-12, 16-21, 23-38, 40-63, 65-67 and 77-91 remain pending and under consideration. The amendments of the claims and the various rejections raised in the Office Action are discussed in more detail below.

II. Amendments

Claim 1 is amended to refer to an isolated nucleic acid, as well as to specify that the nucleic acid is introduced into a rice plant cell expressing the prolamin polypeptide, and the antisense activity reduces the amount of expression of the prolamin polypeptide relative to a rice plant to which the nucleic acid was not introduced, and wherein the nucleic acid is operably linked in antisense orientation to a promoter that functions in a rice plant. Support for this amendment can be found at least in paragraphs [0062] and [0077] of published application US 20080096277, as well as in original claim 81.

Withdrawn claim 23 is amended to parallel claim 1.

Claims 8, 9 and 10 are amended for antecedent basis.

Claim 25 is amended to remove an extraneous comma at the end of the sentence.

Claims 28, 37 and 89 are amended for proper grammar.

No new matter is added by way of these amendments.

III. Rejection under 35 U.S.C. §101 - Non-Statutory Subject Matter

The Examiner asserts that the claims are unpatentable as reading on a naturally occurring DNA molecule *per se* found in nature.

Applicants have amended claim 1 according to the Examiner's suggestion, obviating the rejection. Applicants respectfully request that this rejection be withdrawn.

IV. Rejection under 35 U.S.C. §112, second paragraph

Claims 1, 2, 5, 6, 8 and 9 were rejected under 35 U.S.C. §112, second paragraph as allegedly "incomplete for omitting essential elements."

Specifically, the Examiner alleges that the omitted elements are "the functional elements required for the nucleic acid molecule to have antisense activity."

Claims 1, 2, 5, 6, 8 and 9 were also rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention.

The Examiner alleges that the term "reduces expression" is indefinite, as it does not define a standard for ascertaining the requisite degree, and does not reasonably apprise the skilled artisan of the scope of the claims.

The amendment of claim 1 (supported at least in paragraphs [0062] and [0077] of the published application) obviates both rejections, and Applicants respectfully request withdrawal of these rejections under 35 U.S.C. §112, second paragraph.

V. Rejection under 35 U.S.C § 102

Claims 1, 2, 5, 6, 8 and 9 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Mitsukawa *et al.* (GenBank Accession AB016505 published on 9 January 1999). This rejection is respectfully traversed.

A. The Present Claims

The claims under examination relate to an isolated nucleic acid molecule having antisense activity comprising (i) a nucleic acid sequence having at least 15 contiguous nucleotides complementary to a gene encoding a prolamin polypeptide, or (ii) a nucleic acid sequence having at least 70% homology to (i), wherein the nucleic acid is introduced into a rice plant cell expressing the prolamin polypeptide, and the antisense activity reduces the amount of expression of the prolamin polypeptide relative to a rice plant to which the nucleic acid was not introduced, and wherein the nucleic acid is operably linked in antisense orientation to a promoter that functions in a rice plant.

B. The Cited Art

MITSUKAWA, *ET AL.* is a GenBank nucleotide sequence disclosing a cDNA encoding a rice prolamin polypeptide.

C. Analysis

The standard for lack of novelty, that is, for anticipation, is one of strict identity. According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as it is contained in the claim." *See Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Mitsukawa fails to teach the presently claimed isolated nucleic acid molecule having antisense activity. Mitsukawa further fails to teach a nucleic acid sequence having at least 70% homology. Mitsukawa also fails to teach introduction of such an isolated nucleic acid molecule into a rice plant cell. Finally, Mitsukawa fails to teach that the presently claimed isolated nucleic acid molecule, when introduced into a rice plant, has antisense activity which reduces the amount of expression of the prolamin polypeptide relative to a rice plant to which the nucleic acid was not introduced, and wherein the nucleic acid is operably linked in antisense orientation to a promoter that functions in a rice plant.

Accordingly, Applicants submit that standard of strict identity to maintain a rejection under 35 U.S.C. § 102 has not been met and withdrawal of the rejection under 35 U.S.C. § 102 is respectfully requested.

VI. Rejection under 35 U.S.C. §103

Claims 1, 2, 5, 6, 8 and 9 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Kirihara *et al.* (US Patent No. 6,326,527 issued 4 December 2001) in view of Maruta Y. (US Patent No. 5,516,668 issued on 14 May 1996), further in view of Mitsukawa *et al.* (GenBank Accession AB016505 published on 9 January 1999). According to the Patent Office, it would have been obvious for the skilled artisan to modify the method taught by Kirihara *et al.* inhibiting expression of prolamine in maize to a method of reducing expression of prolamins in rice, using the sequence taught by Mitsukawa *et al.* to make antisense constructs, and would have been motivated to do so because Maruta teaches that reducing the protein content in rice grains helps with processing.

This rejection is respectfully traversed.

A. The Present Claims

The present claims are described above.

B. The Cited Art

KIRIHARA, ET AL. describes modifying the nutritional content of maize using preselected DNA constructs (which can include sense or antisense DNA sequences) to reduce the levels of proteins, such as the abundant prolamine (zein) fraction of seed storage proteins, in transgenic maize plants.

MARUTA describes a method for decreasing seed storage proteins, in particular glutelin proteins, in maize, wheat and barley, by using a nucleotide sequence complementary to the mRNA of glutelin to inhibit its translation.

MITSUKAWA, *ET AL.* IS described above.

C. Analysis

C1. Legal Standard for Determining Obviousness Under 35 U.S.C. § 103(a)

Determining obviousness under 35 U.S.C. § 103(a) requires an objective analysis involving four factual inquiries, which include:

(a) determining the scope and content of the prior art,

(b) ascertaining the differences between the prior art and the claims at issue;

(c) resolving the level of ordinary skill in the art; and

(d) evaluating evidence of secondary considerations.

See Graham v. John Deere, 383 US 17, 18, 148 USPQ 459, 467 (1966); *see also* M.P.E.P. § 2141. A claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1385 (US 2007). It is also important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *See id.* Thus, in assessing the scope and content of the prior art, the references must be considered in their entirety, *i.e.*, each as a whole including portions that would lead away from the claimed invention. *See W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 US 851 (1984); *see also* M.P.E.P. § 2141.02.

Further, the Office examination guidelines following the Court decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1385 (US 2007) indicate that an issue to consider in assessing obviousness is whether a combination of prior art elements yields "predictable results." *See Federal Register*, Vol. 72, No. 195, October 10, 2007.

With respect to the four factual inquiries above, Applicants submit:

(a - b) The scope and content of the cited references differs from the claimed subject matter.

Kirihara *et al.* and Muruta *et al.* are silent with respect to inhibiting expression of rice prolamin as a target, and present not a single nucleic acid molecule that could be used for suppression of rice prolamin.

The Kirihara reference is directed to transgenic maize, failing to teach or suggest reducing expression of the prolamin polypeptide in rice.

The Maruta reference teaches inhibition of translation of the glutein protein in seeds.

As noted above, Mitsukawa *et al.* merely disclose the cDNA cloning, purification and sequencing of six 13kDa prolamin polypeptides from a PB-1 fraction (see section 4 and Figure 4 of Mitsukawa *et al.*). Mitsukawa *et al.* fails to even remotely teach or suggest an antisense construct able to decrease the expression of the prolamin peptide in rice, or even the notion of obtaining such a construct, or an expression cassette thereof, to gain the effect of the presently claimed subject matter. Mitsukawa *et al.* is completely silent with respect to a nucleic acid molecule having antisense activity for reducing expression of the prolamin peptide, and presents no disclosure enabling one skilled in the art to allow one to design an isolated nucleic acid molecule having antisense activity capable of reducing the amount of expression of the prolamin polypeptide in a rice plant relative to a rice plant to which the nucleic acid was not introduced, wherein the nucleic acid is operably linked in antisense orientation to a promoter that functions in a rice plant.

None of the cited references teaches or suggests an isolated nucleic acid molecule having antisense activity comprising a nucleic acid sequence having at least 15 contiguous nucleotides complementary to a gene encoding a prolamin polypeptide. Nor do any of the references teach or suggest a nucleic acid sequence having at least 70% homology to a nucleic acid sequence having at least 15 contiguous nucleotides complementary to a gene encoding a rice prolamin polypeptide.

(c - d) The presently claimed isolated nucleic acid molecule has unexpected and surprising properties, and produces unpredictable results in view of the cited references.

Previous attempts have been made to modify protein content or protein quality of seeds for improving the nutritional value (replacing nutritionally deficient proteins with nutritionally enhanced proteins), taste or processing character. As noted in column 1, lines 27-29 of Kirihara, in maize, the prolamine (zein) fraction of storage proteins comprises over 50% of the total protein in mature seed. In contrast, glutelin is the most abundant protein in rice seeds, an

thus, the main goal has been to produce a "low-glutelin rice linage" (see pages 4 and 5 of the specification as filed). These previous attempts to reduce glutein content have often resulted in concurrent significant increases in prolamin content, which has low nutritional value (page 3, lines 3-5 and page 5, lines 4-14 of the specification as filed). Such research attempts, including the case of Murata *et al.* fail to achieve the purpose. In this regard, please argue that the present inventors through innovative study into the mechanisms of seed storage proteins, found an advantageous solution for providing low protein content seeds, and improving foreign protein expression that can be used to alter the nutritional or economical value of the seed or plant etc. (page 8, lines 26-30 of the English translation of the specification as filed).

The skilled artisan would have no reasonable expectation, in view of the cited prior art, that a reduction in expression of prolamin would successfully achieve a low-protein rice seed. Although the content of prolamin is less than half of that of glutelin in rice seeds, and in spite of the teachings away (1) that glutein (being the major seed storage protein in rice) was the ultimate target for reduction of gene expression, and (2) that reduction of glutein often undesirably increased prolamin expression, Applicants nonetheless chose prolamin as a target for reduction of gene expression. The present inventors unexpectedly found that the introduction of the claimed nucleic acid molecule into rice not only leads to a reduction of expression of prolamin mRNA, but also lead to the marked reduction of the protein amount expressed in seed. This effect had not been found, or even suggested in the state of the art as of the priority date (page 87, lines 1-12 of the specification as filed). Such significant effects can be clearly seen in Example 4 of the specification as filed, which shows that when a prolamin antisense gene was introduced into a general rice variety, the abundance of 13kDa prolamin protein was significantly reduced, and 10kDa prolamin and 16kDa prolamin were also reduced (page 125, lines 25-33 of the English translation of the specification as filed). These results were also confirmed in Figure 3, primarily shown in lanes 4 and 5.

As can be seen from Table 1 of page 128, the antisense constructs of the presently claimed subject matter not only reduced the expression of prolamin, but also have the added value of suppressing or having a neutral effect on other storage proteins (page 129, lines 1-9 of the specification as filed). That is to say, the reduction of prolamin polypeptide upon introduction of the antisense construct into rice did not cause the accumulation of other storage proteins. As a result, protein content of the low-prolamin seed was lower than that of a usual cultivar.

In conclusion, the presently claimed subject matter reduces expression of prolamin polypeptide where reduction of glutelin has failed to produce a low-protein rice seed. (*See* page 126, lines 16-17). Applicants have observed a clear, significant, and unexpected effect in view of the cited references. Thus, the present claims are novel and inventive.

Applicants have also noted evidence of nonobviousness of the claimed subject matter by providing ways in which the claimed combination produces more than could be predicted from the cited references. As noted in M.P.E.P. § 2143.02, in an obviousness determination, the predictability of a technology is determined at the time the invention was made. "Whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986).

For at least these reasons, and in view of the improved performance characteristics achieved with the claimed composition, Applicants submit that the presently claimed subject matter patentably defines over the cited references, and respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

CONCLUSION

In view of the foregoing, claims 1, 2, 4-12, 16-21, 23-38, 40-63, 65-67 and 77-91 are believed to satisfy all of the criteria for patentability and are in condition for Allowance. An early indication of the same is therefore kindly requested.

No fees are believed to be due in connection with this Amendment. However, the Commissioner is authorized to charge any additional fees that may be required, or credit any overpayment, to King & Spalding LLP Deposit Account No. 50-4616.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 590-1932.

Respectfully submitted,
KING & SPALDING LLP

Date: 20 January 2010

/Susan J. Myers Fitch/
Susan J. Myers Fitch
Reg. No. 55,477

Correspondence Address:
Customer No. 79975

KING & SPALDING LLP
333 TWIN DOLPHIN DRIVE
SUITE 400
REDWOOD SHORES, CA 94065
TEL: (650) 590-0700
FAX: (650) 590-1900
WWW.KSLAW.COM